

SYNTHESIS OF 2,2-DIMETHYLBENZOXAZEPINONES BY THE BECKMANN REAR-
RANGEMENT OF 2,2-DIMETHYL-4-CHROMANONE OXIMES¹

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Dedicated to Prof. Dr. E. Pungor on the occasion of his 70th
birthday

Abstract ——— 2,3-Dihydro-2,2-dimethyl-1,4-benzoxazepin-
5(4*H*)-ones and 2,3-dihydro-2,2,6-trimethyl-1,5-benzoxazepin-
4(5*H*)-ones have been synthesized by the Beckmann rearrangement
of 2,2-dimethyl-4-chromanone oximes.

INTRODUCTION

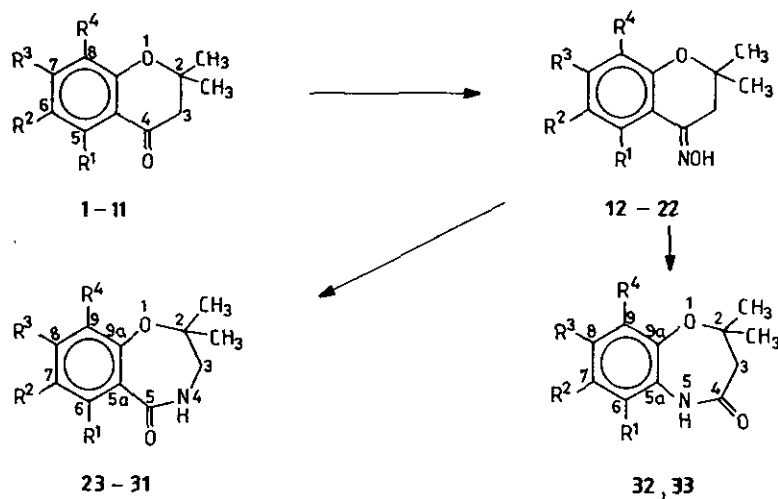
A new synthesis of 2,3-dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4*H*)-ones and 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5*H*)-ones by the Schmidt reaction of 2,2-dimethyl-4-chromanones has been described in our previous paper.² Since the 2,2-dimethylbenzoxazepine derivatives have hitherto got less attention³⁻⁵ it seemed expedient to search various procedures for their synthesis.

2,3,4,5-Tetrahydro-1,5-benzoxazepine derivatives were prepared by the lithium aluminum hydride reduction of 4-chromanone oximes.⁶ Bhalerao and Thyagarajan⁷ obtained 2,3-dihydro-1,4-benzoxazepin-5(4*H*)-ones and 2,3-dihydro-1,5-benzoxazepin-4(5*H*)-ones by the Beckmann rearrangement of 4-chromanone oximes. However, the reason for the formation of 1,4- and/or 1,5-benzoxazepine isomers by such rearrangement of the 4-chromanone oximes has not been thoroughly studied. 2,2-Dimethyl-4-chromanone oximes proved to be convenient model compounds to investigate the influences both of the *E/Z* isomerism of the oximes and the substitution pattern of their aromatic ring on this rearrangement. Furthermore, a comparative evaluation of the synthetic utility of the Schmidt reaction of 2,2-dimethyl-4-chromanones² and the Beckmann rearrangement of their oximes became available in this way.

RESULTS AND DISCUSSION

Chromanone oximes are well known compounds^{6,7} obtained by the reaction of chromanones with hydroxylamine. While from 2,2-dimethyl-4-chromanones only few oxime ethers have hitherto been prepared.^{8,9} For this reason, it was expedient to investigate the synthesis and stereochemistry of the 2,2-dimethyl-4-chromanone oximes utilized for the Beckmann rearrangement. 2,2-Dimethyl-4-chromanones (1 - 11) were refluxed with hydroxylamine hydrochloride in the presence of sodium acetate in ethanol to afford their oximes (12 - 22) in moderate yield (Table 1). Structure and *E/Z* isomerism of oximes (12 - 22) were elucidated by ¹H and ¹³C-nmr data (Tables 2 and 3).

To determine the *E/Z* isomerism of the oximes (12 - 22) ¹³C chemical shift values of the starting 2,2-dimethyl-4-chromanones (1, 5 and 10) and their oximes (12, 16 and 21) (Table 3) have been correlated. The most pronounced changes were observed in the chemical shifts of the C-4 and C-3 atoms. The differences between the chemical shifts of the C-4 (and C-3) atoms for the starting chromanones and those for the major isomers of oximes were 40 (and 15) ppm, respectively. While they were 44 (and 8) ppm for the minor isomers.



- 1, 12, 23: $R^1 = R^2 = R^4 = H$, $R^3 = CH_3O$
 2, 13, 24: $R^1 = R^2 = R^4 = H$, $R^3 = C_2H_5O$
 3, 14, 25: $R^1 = R^2 = R^4 = H$, $R^3 = n-C_3H_7O$
 4, 15, 26: $R^1 = R^2 = R^4 = H$, $R^3 = n-C_4H_9O$
 5, 16, 27: $R^1 = R^4 = H$, $R^2 = R^3 = CH_3O$
 6, 17, 28: $R^1 = R^2 = H$, $R^3 = CH_3O$, $R^4 = CH_3$
 7, 18, 29: $R^1 = R^2 = H$, $R^3 = C_2H_5O$, $R^4 = CH_3$
 8, 19, 30: $R^1 = R^2 = H$, $R^3 = n-C_3H_7O$, $R^4 = CH_3$
 9, 20, 31: $R^1 = R^2 = H$, $R^3 = n-C_4H_9O$, $R^4 = CH_3$
 10, 21, 32: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = CH_3O$
 11, 22, 33: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = C_2H_5O$

All these results prove the *E* structure of the major product in which a γ -steric interaction may occur between the hydroxy group and the C-3 atom.^{10,11} Chemical shifts of the H-5 and H-3 protons are characteristically different in the *E* and *Z* isomers of oximes (see Table 2).¹²

In solution the oximes (12 - 22) may adopt two half chair conformations fast

Table 1. Physical constants and analytical data of compounds **12-35**

Coumpound	mp °C	Yield %	Overall formula	Calculated N %	Found N %
12	129-130	63.3	C ₁₂ H ₁₅ NO ₃	6.32	6.41
13	123-124	86.2	C ₁₃ H ₁₇ NO ₃	5.95	5.86
14	116-117	69.5	C ₁₄ H ₁₉ NO ₃	5.61	5.57
15	93- 94	71.9	C ₁₅ H ₂₁ NO ₃	5.31	5.26
16	112-113	87.6	C ₁₃ H ₁₇ NO ₄	5.57	5.51
17	182-183	65.6	C ₁₃ H ₁₇ NO ₃	5.95	5.99
18	137-138	88.6	C ₁₄ H ₁₉ NO ₃	5.61	5.63
19	139-140	75.0	C ₁₅ H ₂₁ NO ₃	5.31	5.24
20	151-152	66.3	C ₁₆ H ₂₃ NO ₃	5.04	5.08
21	117-118	69.8	C ₁₃ H ₁₇ NO ₃	5.95	5.88
22	86- 87	66.9	C ₁₄ H ₁₉ NO ₃	5.61	5.56
23	137-138 ^a	42.0	C ₁₂ H ₁₅ NO ₃	6.32	6.36
24	130-131	39.0	C ₁₃ H ₁₇ NO ₃	5.95	5.98
25	119-120	35.0	C ₁₄ H ₁₉ NO ₃	5.61	5.55
26	95- 96	31.4	C ₁₅ H ₂₁ NO ₃	5.31	5.37
27	175-176 ^b	36.6	C ₁₃ H ₁₇ NO ₄	5.57	5.62
28	244-245 ^c	43.3	C ₁₃ H ₁₇ NO ₃	5.95	5.92
29	210-211	40.8	C ₁₄ H ₁₉ NO ₃	5.61	5.58
30	190-191	55.0	C ₁₅ H ₂₁ NO ₃	5.31	5.30
31	185-186	36.5	C ₁₆ H ₂₃ NO ₃	5.04	4.98
32	261-262 ^d	29.2	C ₁₃ H ₁₇ NO ₃	5.95	5.93
33	227-228	30.9	C ₁₄ H ₁₉ NO ₃	5.61	5.67
34	129-130	9.3	C ₁₂ H ₁₅ NO ₃	6.32	6.38
35	177-178	4.6	C ₁₃ H ₁₇ NO ₄	5.57	5.64

lit.,² mp [°C] ^a138-139, ^b175-176, ^c244-245, ^d261-262

Table 2. *E/Z* Isomer ratio, ^1H chemical shifts^a and characteristic coupling constants for oximes 12-22 (CDCl_3)

	12	13	14	15	16	17	18	19	20	21	22
<i>E/Z</i>	98/2	95/5	93/7	92/8	94/6	96/4	95/5	95/5	92/8	100/0	100/0
H-3	2.89 (2.54)	2.87 (2.52)	2.87 (2.52)	2.86 (2.51)	2.86 (2.53)	2.84 (2.49)	2.86 (2.50)	2.86 (2.51)	2.87 (2.52)	2.92	2.89
H-5	7.68 (8.62)	7.66 (8.59)	7.66 (8.59)	7.66 (8.60)	7.23 (8.25)	7.63 (8.47)	7.59 (8.48)	7.59 (8.50)	7.60 (8.48)	-	-
H-6	6.50	6.49	6.50	6.49	-	6.50	6.49	6.47	6.48	6.37	6.34
H-8	6.38 (6.40)	6.39	6.37	6.38	6.39 (6.43)	-	-	-	-	6.27	6.23
N-OH	9.58	8.87	8.96	8.60	8.92	7.34	7.89	8.63	7.95	8.33	7.59
Me ₂ -2	1.40 (1.45)	1.40	1.40	1.39	1.39 (1.46)	1.38	1.38	1.39	1.40	1.38	1.42
Me-5	-	-	-	-	-	-	-	-	-	2.52	2.49
Me-8	-	-	-	-	-	2.06	2.07	2.08	2.07	-	-
MeO-6	-	-	-	-	3.85 ^c	-	-	-	-	-	-
MeO-7	3.78 (3.79)	-	-	-	3.86 ^c	3.84	-	-	-	3.77	-
CH ₂ O-7	-	4.01	3.89	3.93	-	-	4.05	3.94	3.98	-	4.00
RCH ₂ O-7 ^b	-	1.40	1.80	1.74	-	-	1.41	1.82	1.78	-	1.36
			1.02	1.47				1.05	1.50		
				0.96					0.98		

Coupling constants (Hz): $J(\text{H-5}, \text{H-6})=8.8$; $J(\text{H-6}, \text{H-8})=2.5$; in the RCH_2O group: $J(\text{H-1}', \text{H-2}')=6.3-6.9$; $J(\text{H-2}', \text{H-3}')=J(\text{H-3}', \text{H-4}')=7.7$ ^a Chemical shifts in brackets correspond to the minor *Z* isomer^b R: Me, Et, Pr^c Tentative assignment

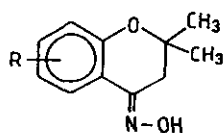
Table 3. ^{13}C Chemical shifts^a of chromanones **1**, **5**, **10**, oximes **12**, **16**, **21**, and of the secondary products **34** and **35** (CDCl_3)

	1	5	10	12	16	21	34	35
C-2	79.2	79.4	78.0	75.8	75.6 (76.7)	75.0	88.4	88.4
C-3	48.2	48.3	48.7	33.6 (40.9)	33.6 (40.7)	34.0	-	-
C-4	190.4	190.7	191.7	149.7 (145.8)	150.1 (146.1)	152.2	164.7	164.5
C-4a	113.8	112.2	112.4	110.0	108.3 (106.1)	109.5	111.1	109.4
C-5	127.3	106.4	143.0	124.7 (132.5)	104.9 (112.9)	139.3	129.4	108.6
C-6	108.8	143.9	111.4	108.8 (107.5)	143.6 (142.1)	111.4	109.5	144.7
C-7	165.8	156.2	163.9	162.4	152.1 (152.4)	160.7	164.7	154.5
C-8	100.8	100.4	99.0	101.8 (101.3)	101.1 (100.4)	99.8	100.5	99.6
C-8a	161.5	156.2	162.7	156.1 (157.0)	149.8 (150.9)	157.2	159.7	153.6
Me ₂ -2	26.3	26.5	26.1	26.8 (26.3)	26.6 (26.1)	26.7	-	-
CH-2	-	-	-	-	-	-	31.5	31.5
Me ₂ -CH	-	-	-	-	-	-	16.2 16.9	16.4 16.9
Me-5	-	-	22.6	-	-	24.6	-	-
MeO-6	-	56.1	-	-	55.8 ^b	-	-	56.2 ^b
MeO-7	55.1	56.1	54.6	55.3	56.0 ^b	55.1	55.5	56.3 ^b

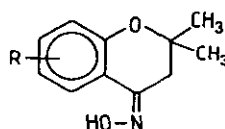
^a Chemical shifts in brackets correspond to the minor *Z* isomer

^b Tentative assignment

interconversion of which results in the appearance of an averaged ^{13}C signal of the two geminal methyl groups and a singlet ^1H signal of the methylene protons. Compounds (12 - 22) were allowed to react with polyphosphoric acid at 50°C and 2,3-dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4*H*)-ones (23 - 31) and 2,3-dihydro-2,2,6-trimethyl-1,5-benzoxazepin-4(5*H*)-ones (32 and 33) have been prepared. On the basis of the known mechanism of the Beckmann rearrangement,¹³ the formation of 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5*H*)-ones were expected from all the oximes (12 - 22) because the *E/Z* isomeric ratio of the starting oximes was approx. 95:5%. To rationalize this apparent contradiction further investigations have been performed. Since the Beckmann rearrangement takes place in acidic medium, it seemed expedient to control the *E/Z* isomeric ratio of the oximes in such milieu by nmr spectroscopy. Our measurements revealed that the initial 5% *Z*-isomer ratio was shifted to approx. 40% in 4:1 mixture of CDCl_3 and trifluoroacetic acid. For this reason, the alteration of the *E/Z* isomeric ratio may result in the formation of the 1,4-benzoxazepine isomer (23 - 31) as a consequence of an alkyl migration.



E



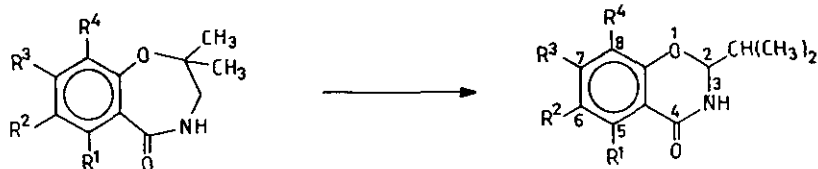
Z

in CDCl_3	95%	5%
in $\text{CDCl}_3:\text{F}_3\text{CCO}_2\text{H}(4:1)$	60%	40%

Whereas in the case of 2,2,5-trimethyl-4-chromanone oximes (10 and 11), owing to the presence of a methyl group in the *peri*-position, such an isomerization is hindered and, therefore, these oximes give 2,3-dihydro-2,2,6-trimethyl-1,5-benzoxazepin-4(5*H*)-ones (32 and 33) on aryl migration. Structure of 2,2-dimethylbenzoxazepinones (23 - 33) has been elucidated by nmr methods.

Characteristic ^1H and ^{13}C -nmr data of compounds (23 - 33) are summarized in Tables 4 and 5. In some cases the assignment of the ^{13}C signals has been corroborated by semiselective INEPT measurements¹⁴ optimized for 7 Hz or 3 Hz long-range couplings (Table 6). Polarization transfer induced from the respective proton indicated the carbon atoms of two or three bond distance from the appropriate proton. The CH_2 signal of the 1,4-benzoxazepines (23 - 31) is doublet as a result of the coupling with the neighbouring NH proton [$J(\text{NH}, \text{H}-3)$ 5.8 Hz] and the δ H-3 value is higher by ca. 0.6 ppm than in the 1,5-isomer. A further characteristic of the 1,4-isomers is that the ^1H signal of the H-6 atom is highly deshielded (δ H-6 7.64 - 7.68) by the *peri*-positioned carbonyl group. ^{13}C Chemical shift values of the C-5a, C-6, C-8 and C-9a atoms of the condensed aromatic ring are characteristically different in the case of the two structural isomers. Since the amide moiety is connected to the aromatic ring by the nitrogen in the 1,5-isomers and by the carbonyl part in the 1,4-benzoxazepines the substituent effects are different¹⁵ and, therefore, in the 1,5-isomers there are downfield shift for the δ C-5a and upfield shift for the δ C-6, δ C-8 and δ C-9a values. The measured ^{13}C chemical shifts are in agreement with those of the analogous 1,4- and 1,5-benzoxazepinones.^{16,17} These ^1H and ^{13}C -nmr measurements made possible an unambiguous differentiation of the synthesized 1,4-benzoxazepinones (23 - 31) and their 1,5-isomers (32 and 33).

Thin-layer (tlc) chromatographic investigation of the reaction mixtures of oximes revealed the presence of small amounts of by-products or secondary products. We managed to isolate 2,3-dihydro-2-isopropyl-1,3-benzoxazin-4-ones (34 and 35) from the crude products of the Beckmann rearrangement of oximes (12 and 16). In the ^1H and ^{13}C -nmr spectra of compounds (34 and 35) an isopropyl group connected to a CH moiety between two heteroatoms was unambiguously identified. Since the C-2 atom of these 1,3-benzoxazinones is a centre of chirality the diastereotopic methyl groups gave signals of different chemical shift values in their ^{13}C -nmr spectra.



23, 27

34: $R^1 = R^2 = R^4 = H$, $R^3 = CH_3O$ 35: $R^1 = R^4 = H$, $R^2 = R^3 = CH_3O$

To elucidate the formation of such 1,3-benzoxazine derivatives, 2,3-dihydro-2,2-dimethyl-8-methoxy-1,4-benzoxazepin-5(4H)-one (23) was treated with polyphosphoric acid at 50 °C similar to the Beckmann rearrangement of oximes and compound (34) was obtained in 18.1% yield. This observation proves that a proton-catalyzed isomerization of 2,3-dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4H)-ones may take place in acidic medium resulting in the formation of 2,3-dihydro-2-isopropyl-1,3-benzoxazin-4-ones as secondary products. On the basis of our present and former² findings, it can be concluded that the Schmidt reaction of 2,2-dimethyl-4-chromanones and the Beckmann rearrangement of their oximes provide similar results in accordance with the known mechanism of these chemical transformations.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Tlc was performed on a Kieselgel 60 F₂₅₄ (Merck) layer using hexane-acetone (7:3 v/v) as eluant. ¹H And ¹³C-nmr spectra were run on a Bruker AC-250 spectrometer at ambient temperature in CDCl₃. Chemical shifts are given on the δ scale.

Table 4. ^1H Chemical shifts and characteristic coupling constants for 1,4- and 1,5-benzoxazepinones (CDCl_3)

	24	25	26	29	30	31	33
$\text{H}_2\text{-3}$	3.11	3.11	3.11	3.08	3.08	3.08	2.46
H-6	7.68	7.68	7.68	7.54	7.55	7.55	-
H-7	6.71	6.72	6.71	6.68	6.68	6.68	6.56
H-9	6.47	6.48	6.47	-	-	-	6.47
NH	8.12	8.17	7.59	7.57	8.06	7.63	7.49
$\text{Me}_2\text{-2}$	1.38	1.38	1.38	1.38	1.38	1.38	1.48
Me-6	-	-	-	-	-	-	2.24
Me-9	-	-	-	2.13	2.14	2.13	-
$\text{CH}_2\text{O-8}$	4.04	3.93	3.97	4.07	3.96	4.00	3.99
$\text{RCH}_2\text{O-8}^a$	1.41	1.81	1.77	1.44	1.84	1.80	1.40
		1.03	1.49		1.06	1.52	
			0.98			0.99	

Coupling constants (Hz): $J(\text{N-H}, \text{H-3}) = 5.8$;

in the RCH_2O group: $J(\text{H-1}', \text{H-2}') = 6.3\text{--}6.9$

$J(\text{H-2}', \text{H-3}') = J(\text{H-3}', \text{H-4}') = 7.7$

$J(\text{H-6}, \text{H-7}) = 8.8$; $J(\text{H-7}, \text{H-9}) = 2.5$

^a R: Me, Et, Pr

Table 5. ^{13}C Chemical shifts of 1,4- and 1,5-benzoxazepinones (23-33) (CDCl_3)

	23	24	25	26	27	28 ^c	29	30	31	32 ^c	33
C-2	85.2	85.2	85.2	85.1	85.3	85.4	85.8	85.9	85.7	85.6	86.5
C-3	49.6	49.6	49.6	49.7	49.6	49.0	49.6	49.5	49.6	44.7	45.3
C-4	-	-	-	-	-	-	-	-	-	170.6	171.7
C-5	171.9	172.0	172.1	171.9	171.9	171.4	172.6	172.7	172.5	-	-
C-5a	120.1	120.0	120.0	119.9	118.7	119.5	120.2	120.1	120.2	124.2	124.2
C-6	131.3	131.3	131.3	131.4	111.3	127.6	128.0	127.8	128.0	131.5	131.7
C-7	110.0	110.5	110.5	110.6	145.3	105.4	106.6	106.5	106.6	110.0	112.5
C-8	163.2	162.7	162.9	163.0	152.3	160.8	160.7	160.7	160.8	156.3	156.8
C-9	108.0	108.5	108.5	108.6	106.2	121.1	121.0	121.0	121.0	106.7	108.2
C-9a	155.4	155.4	155.4	155.4	148.5	152.2	152.8	152.7	152.7	148.3	149.1
Me ₂ -2	24.7	24.7	24.7	24.8	24.6	24.7	25.1	25.1	25.1	26.4	27.2
Me-6	-	-	-	-	-	-	-	-	-	17.4	17.9
Me-9	-	-	-	-	-	8.9	9.4	9.2	9.3	-	-
MeO-7	-	-	-	-	56.0 ^b	-	-	-	-	-	-
MeO-8	55.3	-	-	-	55.8 ^b	55.3	-	-	-	54.7	-
CH ₂ O-8	-	63.6	69.6	67.9	-	-	63.9	69.7	68.0	-	63.7
RCH ₂ O-8 ^a	-	14.5	22.3	31.1	-	-	14.8	22.5	31.3	-	14.7
			10.3	19.1				10.5	19.3		
				13.8					13.8		

^a R: Me, Et, Pr^b Tentative assignment; ^c DMSO- d_6 / CDCl_3 1:1

Table 6. ^1H - ^{13}C Long-range correlations observed by semi-selective 1D INEPT measurements [$J(\text{H},\text{C})=7\text{ Hz}$]

	Proton	Carbon
12	H-3	C-2, C-4, C-4a, Me ₂ -2
16E	H-3	C-2, C-4, C-4a, Me ₂ -2
	MeO-6, MeO-7	C-6, C-7
16Z	H-3	C-2, C-4, C-4a, Me ₂ -2
	H-5	C-4, C-4a, C-6, C-7, C-8a
	H-8	C-4a, C-6, C-7, C-8a
21	H-3	C-2, C-4, C-4a, Me ₂ -2
	MeO-7	C-7
23	H-9	C-5a, C-7, C-8, C-9a
	MeO-8	C-8
27	H-6	C-5, C-5a, C-7, C-8, C-9a
	H-9	C-5a, C-7, C-8, C-9a
	MeO-7, MeO-8	C-7, C-8
28	MeO-8	C-8
	Me-9	C-8, C-9a
	Me-9 ^a	C-9, C-9a
32	H-9	C-5a
	MeO-8	C-8
35	MeO-6, MeO-7	C-6, C-7

^a Semi-selective INEPT optimised for $J(\text{H},\text{C})=3\text{ Hz}$ coupling

General procedure for the preparation of 2,2-dimethyl-4-chromanone oximes (12 - 22)

A mixture of 2,2-dimethyl-4-chromanone (1 - 11: 10.0 mmol), hydroxylamine hydrochloride (1.4 g, 20.0 mmol), sodium acetate (1.6 g, 20.0 mmol), ethanol (40.0 ml) was refluxed for 4 h, cooled to room temperature, the precipitate was filtered and crystallized from methanol to afford compounds (12 - 22) (Table 1).

General procedure for the Beckmann rearrangement of 2,2-dimethyl-4-chromanone-oximes (12 - 22)

A mixture of 2,2-dimethyl-4-chromanone oxime (12 - 22: 5.0 mmol) and polyphosphoric acid (50.0 g) was heated at 50 °C for 1 - 2 h, then cooled to room temperature. The mixture was diluted with water and extracted with chloroform. The organic phase was washed with brine, dried with CaCl_2 , and the solvent was evaporated. The residue was purified by column chromatography to give 2,2-dimethylbenzoxazepinones (23 - 33) (Table 1).

1,3-Benzoxazinones (34 and 35) were obtained as minor component on the column chromatography of the reaction mixtures of the Beckmann rearrangement of oximes (12 and 16).

2,3-Dihydro-2-isopropyl-7-methoxy-1,3-benzoxazin-4-one (34)

A mixture of 2,3-dihydro-2,2-dimethyl-8-methoxy-1,4-benzoxazepin-5(4H)-one (23: 0.44 g, 2.0 mmol) was allowed to react with polyphosphoric acid (10.0 g) as described for compounds (12 - 22) to yield 0.08 g (18.1%) of 34. 34 ^1H -nmr (CDCl_3): 1.13 (d, $J=6.9$ Hz, 6H, $(\text{CH}_3)_2$), 2.15 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 3.83 (s, 3H, CH_3O), 5.07 (dd, $J=1.1$ Hz and 4.7 Hz, 1H, H-2), 6.46 (d, $J=2.5$ Hz, 1H, H-8), 6.62 (dd, $J=1.2$ Hz and 4.9 Hz, 1H, H-6), 7.64 (d, $J=1.1$ Hz, 1H, NH), 7.84 (d, $J=8.0$ Hz, H-5).

35 ^1H -nmr (CDCl_3): 1.12 (d, $J=6.9$ Hz, 6H, $(\text{CH}_3)_2$), 2.13 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 3.90 (s, 3H, CH_3O), 3.91 (s, 3H, CH_3O), 5.05 (dd, $J=1.1$ Hz and 4.7 Hz, 1H, H-2), 6.49 (s, 1H, H-8), 6.56 (d, $J=1.1$ Hz, 1H, NH), 7.34 (s, 1H, H-5).

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